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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,878	09/05/2003	Richard Somberg	03-772	6857

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EXAMINER	
PETERSEN, CLARK D	
ART UNIT	**PAPER NUMBER**
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/655,878	SOMBERG ET AL.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 14 November 2006, in which claims 7, 8, 11, 13, 14, 15, and 21 were amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New rejections are presented in this Office Action; hence this Office Action is NOT FINAL.

Priority

Examiner asserted in the previous Office Action that provisional application 60/408662 did not provide adequate support to receive the priority date of 6 September 2002, the date on which the provisional application was filed. This argument was based on the assertion that the provisional application did not teach sequential addition of reagents but rather that the order of reagent addition was unimportant to the eventual measurement of luciferase activity. This assertion is supported by paras [0015] which states "the order of addition is not critical so long as the kinase has sufficient opportunity to interact with the substrate" and [0034] which describes real time detection wherein a kinase and luciferase reporter are added simultaneously.

However Applicants cite the use of proprietary reagents in paras [0043] to [0049], which are covered by Patent Application WO 02/066671. Based on working examples employing sequential addition of reagents, in which the second reagent includes a

transferase quenching reagent, the assertion that provisional application 60/408662 does not provide support for the instant claims is withdrawn.

Specification Objections

Examiner had objected in the previous Office Action to the inclusion of an embedded hyperlink, specifically at p. 15 line 5 of the instant application. Based on Applicants' amendment to the specification, this objection is withdrawn.

Claim Objections

Examiner had objected in the previous Office Action to apparent improper dependency of claims 7, 8, and 14, and to claim 16 for failing to further limit claim 15. Based on Applicants' amendment to these claims, these objections are withdrawn.

Response to Arguments - 35 USC § 112

Examiner rejected claims 11 and 21 in the previous Office Action as being indefinite.

Based on Applicants' amendment, the rejection of claims 11 and 21 as being indefinite is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 13-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 14, 43-45, 48-51, 55-58 of U.S. Patent No. 7,083,911, issued 1 Aug 2006, and assigned to Promega Corporation.

This is a new rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they recite essentially the same method steps and recite addition of the same reagents.

Claim 1 of US 7,083,911 B2 recites adding a reagent composition comprising detergents and a luciferase, wherein the mixture maintains luciferase activity but the ATPase activity endogenous to the sample is reduced. These limitations encompass

the recitations of claims 1 and 4 of the instant application, in which a sample is contacted with a reagent mixture that comprises a stopping solution that stops transferase activity (which is an ATPase activity) but which leaves luciferase activity stable. Regarding the ATPase activity in the sample, the specification of US 7,083,911 B2 expressly suggests that the term "sample" should be interpreted in the broadest possible sense (see col. 8, lines 4-15). Additionally, when the sample is a cell (a limitation suggested in claim 6 of US 7,083,911 B2), it inherently contains kinase activity, as acknowledged at col. 7, lines 43-50, for example. Claim 43 also recites all the limitations of instant Claim 1 as well as instant Claim 2, in that it recites the use of cells which contain transferase activity, a substrate and ATP, as well as another compound for screening. Claim 55 recites the limitations of instant Claim 3, in that it suggests screening a library of compounds. Claims 13 and 14 recite the limitations regarding detergents of instant claims 13-15.

Additionally, while not claimed, the specification of US 7,083,911 B2 suggests that the detergent sulfobetaine 3-10 is a preferred ATPase quenching agent (see col. 5, lines 38-52, for example). While not claimed, the specification also suggests the addition of divalent metal ion chelating agents – of which EDTA and EGTA are well known examples in the art - as components of ATPase quenching agents (see col. 15, lines 32-49, for example), reading on instant claims 19 and 20. While not claimed, the specification suggests the use of a thermostable luciferase (see col. 14, lines 1-12, for example), reading on instant claim 23.

Response to Arguments - 35 USC § 102

Applicants traverse the rejection of claims 1-8, 19-20, and 22-26 under 35 USC 102(e) as being anticipated by Crouch et al (US Pat App. No. US2004/0253658A1). Applicants assert that Crouch does not teach addition of a reagent comprising a transferase-quenching agent, a luminogenic molecule and a bioluminescence-generating enzyme to a first reaction mixture comprising a transferase, ATP and a transferase substrate. Rather, Crouch teaches the sequential addition of (a) a transferase-quenching reagent followed by (b) a bioluminescence-generating mixture.

Examiner acknowledges that nowhere in the Crouch reference is it expressly stated that the transferase-quenching reagent should be combined with the bioluminescence-generating mixture in a single composition. Therefore, based on Applicants' arguments, the rejection of claims 1-8, 19-20, and 22-26 under 35 USC 102(e) is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al (US Pat App. No. US2004/0253658A1).

This is a new rejection.

This is the rejection provided in the previous Office Action under 35 USC 102(e).

Crouch et al teach a method of detecting kinase activity. This method comprises combining a kinase, ATP and substrate for the kinase and allowing an enzymatic reaction to occur. They teach that the enzymatic reaction solution also comprises a luciferase enzyme and a luciferin, and that by measuring the bioluminescence of the solution, one can determine how much ATP was consumed by the kinase reaction, and therefore the activity of the kinase (see Abstract; see claims 43 and 44, as examples). Crouch et al also teach that the kinase reaction can be allowed to proceed for a certain amount of time before the addition of the luciferase and luciferin (see p. 3 para [0061], for example). They teach that when allowing the kinase reaction to proceed for a period of time before adding luciferase/luciferin, it is advantageous to first stop the kinase reaction with a stopping solution (see p. 4, para [0069], for example).

Crouch et al teach that this method is useful for identifying compounds which can modulate kinase activity (see p. 3, para [0046], for example).

Crouch et al also teach that this method is useful for high-throughput screening of compounds that might influence kinase activity (see p.4-5, para [0085] for example).

Crouch et al also teach working examples of specific kinases for which this method is applicable. For example MAPK can be tested (see p. 6, Example 2, paras. [0106]-[0110], for example) for its ability to phosphorylate its substrate Myelin Basic Protein, and also MEK can be studied for its ability to phosphorylate its substrate MAPK(see p. 7, Example 7, paras. [0115]-[0116], for example).

Crouch et al also teach that the solution for stopping the kinase reaction before addition of the luciferase/luciferin can be EDTA or EGTA, because luciferase is somewhat more resistant to these metal chelators than enzymes generally (see p. 4, paras. [0069] and [0070], for example).

Crouch et al also teach that it is advantageous to use a thermostable luciferase in their method (see p. 4 para [0074], for example).

Crouch et al also teach that, in a method of studying a compound's influence on a kinase's activity, the effect can be either an inhibition or an activation of the kinase (see p. 3, paras [0053]-[0058], for example).

Crouch et al teach that many compounds can be used as stopping agents, and need not be limited to EGTA, EDTA, or phosphoric acid (see p. 4, para [0072], for example). Additionally, Crouch et al teach that staurosporine is an effective kinase inhibitor that does not seem to affect luciferase activity (see p. 12, Example 14, paras. [0206]-[0212], for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to incubate a first reaction mixture containing a transferase, ATP, and a substrate for a period of time, followed by adding a second solution comprising a stopping agent, a luminogenic molecule and a bioluminescence-generating enzyme because Crouch et al teach that it is advantageous to allow a transferase reaction to proceed for some time before adding luminogenic molecules, and adding a stopping solution before measurement gives the artisan more precision in measuring the transferase activity .

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to allow a transferase reaction to proceed for some time before adding a stopping solution and a bioluminescence-generating mixture.

Claims 1-8 and 13-17 and 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991).

This rejection is based partly on the rejection over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991) discussed in the previous Office Action, and included below.

However, based on Applicants' amendment, the rejection has been expanded to include claims 15 and 17 which as previously written were determined to be free of the art.

The teachings of Crouch et al are discussed above and applied as before.

Crouch et al do not expressly teach the addition of kinase reaction stopping agents that comprise detergents.

However Simpson et al studied the effects of various types of detergents on the biochemical kinetics of the luciferase/luciferin reaction. They studied anionic, nonionic, and cationic detergent types and measured stability of the luciferase enzyme, rate of reaction, and whether detergents increased or decreased the luminescent signal detected from the reaction (see Materials and Methods; see Table 1, p. 100, as examples).

Specifically they test the effects of sodium dodecyl sulfate (SDS), dodecyltrimethylammonium bromide, and cetyltrimethylammonium bromide on luciferase activity, and beneficially report that SDS does not interfere with luciferase activity, and dodecyltrimethylammonium bromide, and cetyltrimethylammonium bromide temporarily increase the stimulation of luciferase (see Table 1, p. 100).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a secondary solution comprising luciferin, luciferase and a detergent in a method of detecting transferase activity taught by Crouch et al, because Simpson et al teach that it is possible to add a detergent to a solution containing components of a luciferase/luciferin ATP assay system, and detect measurable light signals. One would have been motivated to do so because Simpson et al point out that the possibility exists – and they subsequently demonstrate – that detergents have an ability to stimulate luciferase activity and thus could be used to reduce assay costs or to increase assay sensitivity (see p. 98, col. 1, for example).

Based upon the teachings of the cited references and the level of skill of one of ordinary skill in the art, there would have been a reasonable expectation of success in practicing the claimed invention.

Response to Arguments - 35 USC § 103

Applicants have argued, regarding rejections under both 35 USC 102(e) and 35 USC 103(a) in the previous Office Action, that Crouch et al fail to suggest the invention of the instant application because they teach that one should add stopping buffer as a separate step before adding the bioluminescence-generating mixture.

This argument has been fully considered but is not deemed persuasive.

Crouch et al teach that it is advantageous to allow the transferase reaction to proceed for some amount of time before adding a stop buffer and bioluminescence-generating mixture. Crouch et al expressly teach that the stop buffer need not interfere with the bioluminescence-generating enzyme. They teach that EDTA is a useful stopping agent because luciferase, unlike most enzymes, is resistant to its inhibitory effects (see para [0070], for example). They also suggest the use of pH stable luciferases which can function to generate useful data in the presence of acidic pH which is used for stopping transferase activity. They expressly note that there is no need for adjusting the reaction mixture when a pH-stable luciferase is used (see para [0074], for example).

Regarding Applicants' argument that Crouch et al teach away from combination of stopping agent with bioluminescence-generating mixture, this step is only suggested for the convenience of the operator, not as a step essential to properly obtaining data from the assay (see para [0072], for example).

Based on the teachings of Crouch et al that luciferases can properly function in the presence of chemicals that inhibit transferase activity, it would be equivalent to

include the luciferase/luciferin with the stopping agent in a single composition, rather than adding the two in separate steps.

Applicants traverse the rejection of claims 1-10, 19-20, and 22-26 under 35 USC 103(a) as being unpatentable over Crouch et al (US Pat App. No. US2004/0253658A1) in view of Briggs et al (Biochem, 2000). Applicants argue that the combined teachings of Crouch et al and Briggs et al fail to suggest the invention of the instant application.

This argument has been fully considered but is not deemed persuasive.

For the reasons discussed above regarding the rejection of claims 1-8 and 19-26 as being unpatentable over Crouch et al, the rejection of claims 1-10, 19-20, and 22-26 as being unpatentable over Crouch et al in view of Briggs et al is maintained.

Applicants traverse the rejection of claims 1-8, 11, 19-20, and 22-26 under 35 USC 103(a) as being unpatentable over Crouch et al (US Pat App. No. US2004/0253658A1) in view of Lev et al (EMBO J, 1991). Applicants argue that the combined teachings of Crouch et al and Lev et al fail to suggest the invention of the instant application.

This argument has been fully considered but is not deemed persuasive.

For the reasons discussed above regarding the rejection of claims 1-8 and 19-26 as being unpatentable over Crouch et al, the rejection of claims 1-8, 11, 19-20, and 22-26 as being unpatentable over Crouch et al in view of Lev et al is maintained.

Applicants traverse the rejection of claims 1-8, 13-14, 16, 19-20, and 22-26 under 35 USC 103(a) as being unpatentable over Crouch et al (US Pat App. No. US2004/0253658A1) in view of Simpson et al (J Biolum and Chemilum, 1991). Applicants argue that the combined teachings of Crouch et al and Simpson et al fail to suggest the invention of the instant application.

This argument has been fully considered but is not deemed persuasive.

Applicants argue that Simpson et al teach away from the use of detergents in many cases. For example addition of cationic detergents must be of a specific concentration and such detergents also tend to destabilize luciferase. However use of such detergents would be advantageous because Simpson et al teach that the reaction rate of luciferase-catalyzed reactions can be significantly increased, leading to more intense signal (see Fig. 2; see "Cationic Detergents", col. 2, p. 101). Eventual inactivation of the luciferase enzyme is irrelevant, because the reaction mixture is not typically reused in practice standard in the art.

Applicants also assert that Simpson et al caution against the use of detergent, especially non-ionic detergents, due to the unpredictable effect of detergent on luciferase activity, and quotes Simpson from page 103, right column, to that effect. However Simpson et al state that because non-ionic detergents can increase the reaction rate of luciferase-catalyzed reactions, it is "prudent to examine the possibility of incorporating non-ionic detergents into luciferase preparations and thereby reducing the amount of firefly luciferase used in each assay without reducing light output" (p. 103, col. 1). As Applicants assert, Simpson indeed states that variability makes

"supplementation of firefly luciferase preparations with non-ionic detergents ... not currently a viable option". However the reason he gives for this statement is not with detergents themselves but rather with contaminants such as oleic acid (see p. 103, col. 2). They also state that non-ionic detergent can be added to individual assays to advantage as opposed to luciferase stocks themselves (see p. 103, col. 2, last sentence).

Conclusion

No claims are allowed.

Because Examiner has introduced new grounds for rejection, this action is NOT FINAL.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
1/29/2007

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SUPERVISORY PATENT EXAMINER